

# HERPETIC URETHRITIS\*

BY

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The localization of herpetic lesions in the urethra has been recognized since the end of the 19th century. Thus, according to Harkness (1950), Diday and Doyon (1876) were probably among the first to observe this possible aetiology in cases of urethritis. In spite of the comparatively early date of this observation and the abundant literature on this field of pathology, the number of known cases of herpetic urethritis is very small (Callomon, 1924; Scherber, 1935), its study—clinical, anatomic-pathological, and bacteriological—being still in a rudimentary stage.

The facts concerning this localization of herpetic infection may be summed up as follows. The disease generally becomes apparent after normal or buccal sexual contacts, and less often in the course of a febrile disease. Urethral secretion is not usually abundant, and it can be the only symptom of the disease or co-exist with subjective phenomena of variable intensity, from a slight smarting sensation to intense pain on passing urine. Oedema of the meatus may be present, as well as painful swelling of regional lymphatic vessels and ganglia.

In many of the cases described, urethritis co-exists with typical herpetic vesicular lesions in the genital organs, localized in the vicinity of the urethral meatus. There have been cases, however, where the herpetic vesicles were found only inside the urethra.

The appearance of the secretion is similar to that of non-bacterial urethritis: mucus, a few epithelial cells, a few pus globules, and scanty extra-cellular micro-organisms. Urethroscopic examination (Bettmann, 1902, cited by Harkness, 1950) reveals the existence of sparse vesicles, superficial ulceration of the urethral mucous membrane, and occasionally marked congestion with haemorrhagic points (Coutts, 1948, cited by Harkness, 1950).

The disease develops in a few days and often disappears spontaneously along with the extra-urethral herpetic lesions; it has an equal tendency to relapse.

Two cases in which urethral constriction set in

after various attacks of the disease are described in the literature, but Harkness (1950) denies that this complication can be due to the herpetic infection, which is essentially superficial and leaves no scars.

We were unable to find references in Harkness's work to any anatomic-pathological studies; as far as the bacteriological aspect is concerned, he states only that the cultures are sterile in the usual media. In two of his own cases search for agents of the pleuropneumonia type gave a negative result.

Scherber (1935) relates that Durand and Deleuil (1931) succeeded in causing herpetic lesions in the cornea of rabbits by means of the urethral secretion.

## Case History

**Male, aged 27**, single, healthy, and of good constitution; personal and family history irrelevant.

The disease appeared on March 15, 1949, when after comparatively frequent indulgence in coitus during the week before, he began to feel a smarting sensation on micturition which became more intense towards the evening. The next morning he experienced an intense smarting sensation accompanied by a burning pain, and a slight yellow purulent discharge appeared. Believing that he was suffering from gonorrhoea, he took "Elkosin" (a sulphonamide preparation), four tablets at first and then two tablets every 4 hours.

**March 17.**—Symptoms more marked, discharge more abundant.

4 p.m.: 300,000 units procaine penicillin.

12 midnight: 100,000 units procaine penicillin.

**March 18.**—Elkosin treatment suspended by 12 noon.

6 p.m.: 300,000 units procaine penicillin.

**March 19.**—Intense burning sensation on passing urine, discharge similar to previous day.

3 p.m.: begins aqueous penicillin 100,000 units every 3 hrs.

Swab reveals abundant pus cells but no bacteria.

**March 20.**—No improvement. Penicillin discontinued after total of 900,000 units.

**March 21.**—"Irgafen" (another sulphonamide preparation), two tablets every 6 hrs. Towards evening temperature subfebrile 37° 5', slight cutaneous hyperaesthesia especially on the back, pain in the calves, upper limbs, and posterior part of the head. Definite signs of bladder and rectal urgency, and sensation of weight in the lower abdomen. Urethra very sensitive to palpation, no inguinal ganglia.

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*March 22.*—Thinking he has an attack of influenza, patient discontinues "Irgafen", gives himself an intravenous injection of 500 mg. "Redoxon" (ascorbic acid B.P.), and takes "Kina-Redoxon" tablets. Temperature 37°4'; cutaneous hyperaesthesia still present.

*March 23.*—Temperature normal, hyperaesthesia improved.

*March 24.*—On washing with soap and water, patient notes sensitivity of mucous tissue of glans and five small superficial vesicles on the prepuce, near the meatus. Borders of the latter very much congested and slightly ulcerated, though scarcely infiltrated. Thick purulent greenish yellow discharge. Urethral tract was sensitive, no painful inguinal ganglia, slight rectal tenesmus. Swabs of the secretion from the lesions were examined under dark-ground illumination and cultured on blood-agar plates, with negative results.

*March 28.*—Wassermann blood test negative. Symptoms modified, burning sensation during micturition almost disappeared but discharge more abundant. Preputial ulcers improved after washing with solution of permanganate 1:10,000 and application of sulphonamide powder.

*April 4.*—Very intense general cutaneous hyperaesthesia.

*April 8.*—Hyperaesthesia slightly better.

*April 11.*—Discharge better. Negative dark-ground examination of preputial ulcers, which had reappeared. Inoculation of urethral secretion into the chorio-allantoic membrane of chick embryo.

*April 27.*—Ulcers and discharge greatly improved.

*May 4.*—Further improvement.

*May 9.*—Smallpox vaccination carried out, with slight positive reaction.

*May 10.*—Patient almost cured.

*May 20.*—Urethral discharge gone, some mucous threads in urine, some urethral sensitiveness still present, with occasional relapse.

The disease cleared up without giving rise to any further symptoms or complications.

## Discussion

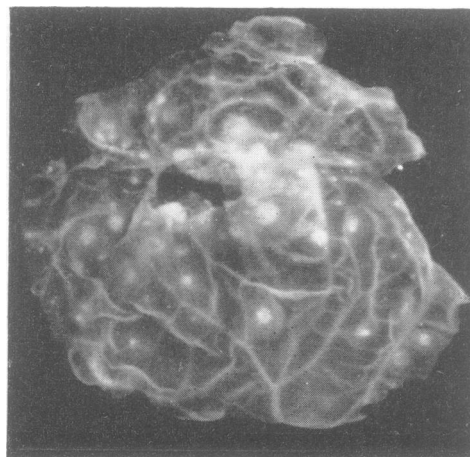
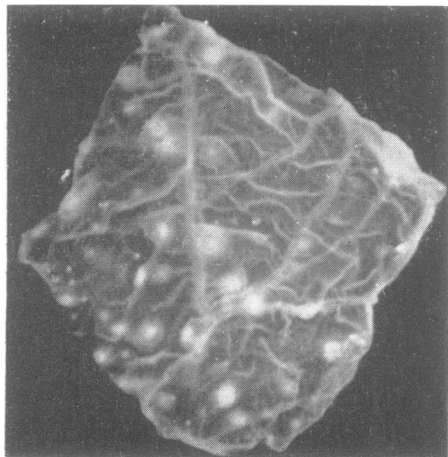
The initial smarting sensation on passing urine was soon followed by a slight purulent yellow discharge akin to gonorrhoea. The following symptoms were noted: absence of adenitis, slight fever attack, intermittent cutaneous hyperaesthesia, negative routine bacteriological examinations, resistance to chemotherapy (penicillin, sulphonamides, antiseptics). After one week the smarting had nearly disappeared, though the secretion was more abundant, and five small superficially ulcerated vesicles appeared on the foreskin and around the urinary meatus. Routine bacteriological examinations were negative. The symptoms were present for about 2 months, and then slowly subsided.

*Bacteriological Study.*—The urethral exudate was treated with penicillin and streptomycin and inoculated into the chorio-allantoic membrane of White-Leghorn eggs with 12 days' incubation. The usual technique of exposure of this membrane through the natural air chamber of the fertilized egg was followed.

The eggs were opened 4 days later; two of the inoculated membranes had intense oedema and a few very small round whitish lesions scattered over the centre of the membrane. The remaining membrane had only slight oedema.

The membranes were removed, ground in a mortar, made up in a 10 per cent. suspension in buffered saline to which penicillin and streptomycin were added, and inoculated into 12 days' incubation eggs.

When these eggs were opened after 3 days, the chorio-allantoic membranes had opaque whitish lesions, most of them rounded and slightly prominent, and were also oedematous (Figs 1 and 2).



FIGS 1 and 2.—Herpetic virus colonies in the chorio-allantoic membrane.

FIG. 3.—Chorio-allantoic membrane. Haematoxylin and eosin.  $\times 102$ .

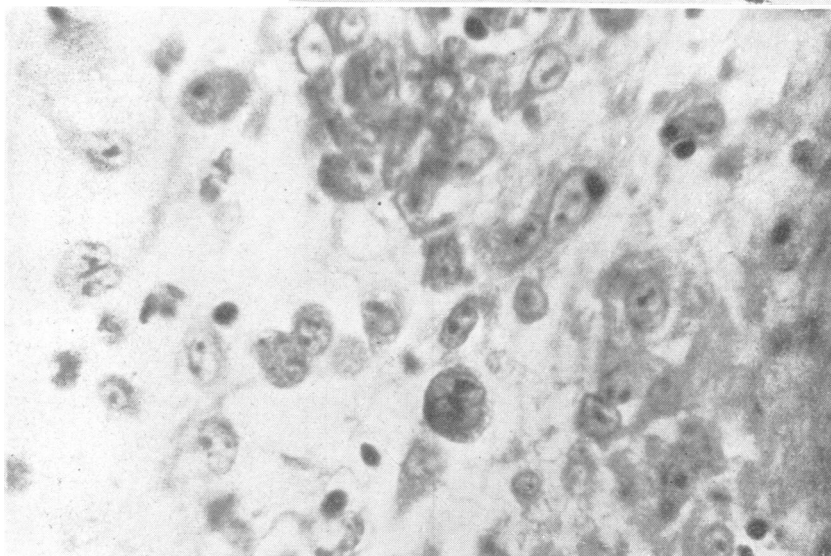
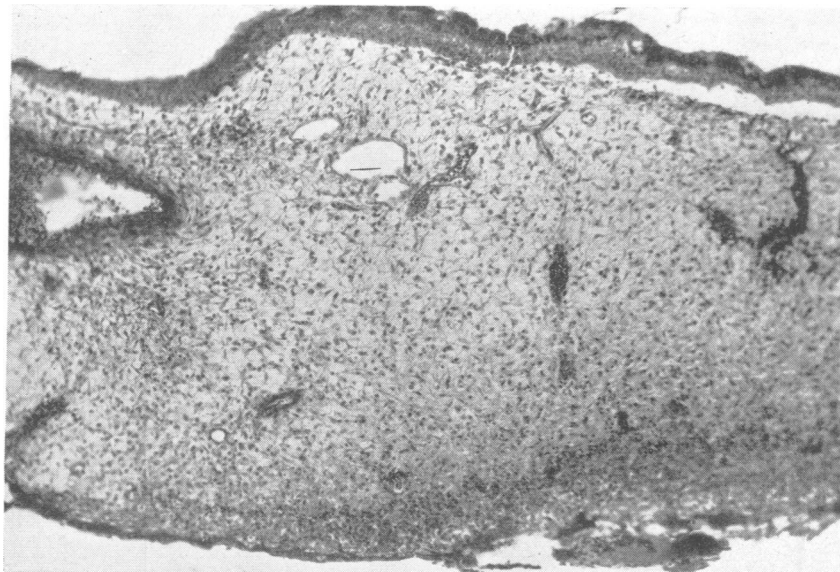


FIG. 4.—Inclusion bodies.  $\times 1030$ .

A second passage into other eggs was performed, and by this time there were multiple lesions similar to those described above. Fragments of the membranes were collected and sent to the histological department.

The isolated virus grows easily in the chorio-allantois, producing the same type of colonies throughout successive passages. In view of the macroscopical lesions observed, we thought of the possibility of herpetic virus.

The histological sections stained with haematoxylin-eosin and with Giemsa revealed intense

lesions of the membranes (Fig. 3) with great proliferation of the ectodermal and mesodermal layers, neoformation of vessels, haemorrhages, marked oedema of the mesoblast, and Lipschütz's bodies in the nuclei of various cells (Fig. 4). In other membranes there were somewhat amorphous eosinophil granules within the nuclei of the cells, which exhibited more or less intense necrosis.

The type of lesions observed in the chorio-allantoic membranes, as well as the presence of intranuclear bodies (Lipschütz's bodies) in the cells affected by the virus, seemed to us evidence of

an herpetic virus infection. It seems unlikely that the lesions observed in the chorio-allantoic membranes were due to any other viruses capable of causing similar infections. No cytoplasmic inclusion bodies were found in the infected cells, as happens in vaccinia virus infections, nor was the virus isolated starting from a conjunctival exudate, which would lead to a differential diagnosis from the kerato-conjunctivitis virus.

The serum neutralization test with anti-herpetic immune serum confirmed the diagnosis. Suspensions of the virus made up in saline at various dilutions put in contact with specific immune rabbit serum incubated at 37° C. for 30 minutes did not cause lesions in the chorio-allantoic membranes, while the controls gave numerous typical lesions.

*Commentary.*—This infection seems to have had a sexual origin; it manifested itself at first by non-bacterial urethritis, in the course of which cutaneous lesions (of the type of genital herpes) appeared on the glans penis, and marked cutaneous hyperaesthesia was experienced. The disease progressed in an undulating form, had two periods of relapse and cleared up spontaneously. Bacteriological examination confirmed the presence of herpetic virus in the urethral secretion.

It is of interest to stress the following facts when the symptoms and the evolution of the disease are taken together:

(1) Direct contagion of a sexual nature. The patient had never suffered from herpes before, and after this attack never revealed any localized infection of the disease.

(2) The urethral meatus and the anterior urethra were the gateway to infection.

(3) Starting from the anterior urethra, there appeared on the one hand a cutaneous localization

(herpetic vesicles), possibly due to direct cutaneous inoculation of the neighbouring region, and on the other hand cutaneous hyperaesthesia, probably due to the spread of the virus to the nervous system.

(4) The disease progressed in an acute form (though without high temperatures) in two stages and cleared up without relapse.

(5) It was possible to isolate the herpetic virus, a fact which so far we have found no other reference in the literature.

### Summary

Herpetic infection of sexual origin in a 27-year-old man started with non-bacterial urethritis which did not subside after the common antibiotic and chemotherapeutic treatments, and revealed in its evolution typical lesions of herpes near the urethral meatus, and marked cutaneous hyperaesthesia especially in the trunk.

The disease developed for 2 months in an undulating form and was cured without relapse.

By inoculation onto the chorio-allantoic membrane of chick embryo it was possible to isolate the herpes virus from the urethral secretion.

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